

METHODS AND COMPOSITIONS FOR
MODULATING CNTF ACTIVITY

ABSTRACT OF THE DISCLOSURE

5 Methods and compositions for altering, or modulating CNTF activity by
altering or modulating cytokine inhibitor activity are provided. Specifically
encompassed are methods and compositions to alter activity of cytokine inhibitors such
as SOCS-1, -2, and -3. SOCS-3 expression is rapidly induced by CNTF treatment in
regions of the hypothalamus that are known to be involved in the regulation of body
10 weight. As described herein, a SOCS-3-mediated CNTF cell-signaling inhibitory
pathway exists, suggesting that SOCS-3 is a negative regulator of CNTF
signal-transduction in the brain. Since CNTF treatment of animals suppresses appetite
and induces weight loss, inhibition of SOCS-3 expression or activity is a potential target
for the development of drugs aimed at improving CNTF sensitivity or prolonging CNTF
15 activity in a mammal and inducing weight loss. Thus, altering SOCS-3 activity
provides a means for modulating CNTF-induced cell signaling and therefore modulating
bodyweight.

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